SOME VARIABLES AFFECTING SINGLE ALTERNATION IN HIPPOCAMPALLY LESIONED RATS

By

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Rats were trained on a single-alternation go, no-go task with either a 10- or 50-second inter-trial interval (ITI). After reaching criterion, the rats were given either bilateral hippocampal lesions, bilateral cortical lesions, or a sham operation. Following recovery, the animals were again tested on the single-alternation task with either a 10- or 50-second ITI. The results were analyzed in terms of three hypotheses that might account for the performance deficit produced by hippocampal lesions in a previous study (Walker, Messer, Freund, & Means, 1972). The results provide the greatest support for the hypothesis that bilateral hippocampal damage decreases the length of time information can be held in short-term memory. However, the data also indicate that none of the three hypotheses can fully explain the performance of the hippocampal animals on the alternation tasks used in this study.

INTRODUCTION

Functions of the Hippocampus

The great amount of research done on the hippocampus in the last thirty-five years has lead to its implication in a large number of behavioral processes, e.g., emotion (Papez, 1937), species preservation (MacLean, 1958), memory (Penfield & Milner, 1958), orienting responses (Grastyan et al., 1959), sequencing of behavior (Kimble & Pribram, 1966), motivation (Peretz, 1965), error registration (Douglas & Pribram, 1966), and behavioral inhibition (Kimble & Kimble, 1965; Kimble, 1968). The two hypotheses of hippocampal function that appear to be the most interesting, at least in terms of the amount of research they have generated, are memory formation and behavioral inhibition.

For example, studies from research using every methodology known to the physiological psychologist, when employed in the study of hippocampal function, have at one time or another resulted in the suggested involvement of the hippocampus in the formation of memory: bilateral hippocampectomy in humans (Scoville & Milner, 1957), protein analysis of the hippocampus following training in rats (Hyden & Lange, 1970), electrical recordings from the hippocampus during the development of conditioned reflexes in cats (Grastyan et al., 1959), bilateral injection of antibiotics into the

hippocampus in mice (Flexner et al., 1963), hippocampal lesions and ECS in rats (Hostetter, 1968) and bilateral electrical stimulation of the hippocampus in rats (Erickson & Patel, 1969).

The earliest and now classic statement of the relationship between memory and the hippocampus was made by Scoville and Milner (1957) when they described a quite dramatic anterograde amnesia following bilateral temporal lobe resections that involved substantial portions of the hippocampus in humans. Their study of one patient in particular, H. M., suggested that the amnesia resulted from an inability to consolidate new experience into a long-term memory store (Penfield & Milner, 1958; Milner, 1959; Milner et al., 1968; Milner, 1968).[1]

Unfortunately, as is well known, the subsequent proliferation of animal studies employing bilateral hippocampal lesions did not substantiate the memory deficit observed in human patients. For example, hippocampectomized animals have demonstrated normal acquisition of a simultaneous brightness discrimination (Schmaltz & Isaacson, 1966) and facilitated acquisition on CRF (continuous reinforcement) training (Kimble, 1963), two-way active avoidance (Isaacson et al., 1961), two-bar alternation (Jackson & Strong, 1969) and single-alternation go, no go (Brown et al., 1969).

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[1]Subsequent research by Corkin (1968) has revealed that patients suffering from bilateral medial temporal lobe resection are capable of acquisition and retention of selected motor skills such as the Rotary Pursuit.

The other major hypothesis of hippocampal function that has received a great deal of attention is that the hippocampus mediates or is in some way responsible for the ability of an animal to inhibit behavior. The behavioral inhibition hypothesis originated from observations of response perseveration in a variety of situations by animals with bilateral hippocampal damage. For example, hippocampal animals show an inability to shift response sets as indicated by deficits in performance on spatial discrimination reversals (Brown et al., 1969; Mahut & Cordeau, 1963), brightness discrimination reversals (Kimble & Kimble, 1965), and tactual discrimination reversals in the cat (Webster & Voneida, 1964). In this regard, it is also interesting that Franchina and Brown (1971) have found that hippocampal animals did not change performance (running speed) in accordance with a change in reward magnitude while their pre-shift acquisition performance remained as sensitive to the magnitude of reward as normals.

Hippocampally lesioned animals also have difficulty in withholding responses as measured by inferior performance on acquisition of DRL (differential reinforcement of low levels of responding) (Clark & Isaacson, 1965; Schmaltz & Isaacson, 1966) and passive avoidance tasks (Isaacson & Wickelgren, 1962; Snyder & Isaacson, 1965). And finally, Hippocampectomized animals demonstrate an increased resistance to extinction (Jarrard et al., 1964; Jarrard & Isaacson, 1965; Kimble, 1968) and a deficit in spontaneous alternation

(Roberts et al., 1962). Consequently, the deficit seen in animals with bilateral hippocampal damage has been described as a response inhibition deficit.

It is again unfortunate that, as with the memory hypothesis, the response inhibition theory is also contradicted by those studies which show facilitated acquisition on two-bar alternation (Jackson & Strong, 1969) and single-alternation go, no-go (Brown et al., 1969) designs, since the performance of these tasks requires that the animal suppress responses.

Single Alternation Go, No Go

Because of the contradictory data and the importance of the memory formation and behavioral inhibition theories of hippocampal function, Means et al. (1970) undertook the study of single-alternation go, no-go acquisition following bilateral lesions of the hippocampus in rats. They used two dependent variable measures, the number of responses per trial and the latency to the first response on each trial. The response measure on no-go trials was to be indicative of the animals' ability to suppress responses (response inhibition) while the latency measure was to indicate the animals' ability to remember what happened on the preceding trial (memory). The response measure was reported as the ratio of the total number of responses on no-go trials/the total number of responses on go trials. The latency measure was reported as the ratio of the total latencies to the first bar press on go trials/the total latencies to the first bar press on no-go trials.

Animals were given either bilateral hippocampal lesions, bilateral cortical lesions, or no operations. Following magazine and CRF training, all animals were trained for 33 days with 20 trials a day on a single-alternation go, no-go task with a 10-second ITI (inter-trial interval).

Several interesting observations resulted from this experiment. First, and most importantly, the hippocampal animals acquired the task significantly faster than either the corticals or normals as indicated by both the response and latency ratios. The improvement observed for both the corticals and normals during acquisition was due only to a gradual decrease in the latency on go trials and an increase in the number of responses on the go trials and not to any improvement in withholding responses on the no-go trials. This facilitation is particularly interesting since other researchers have found the performance of hippocampal animals to be inferior on tasks that also require successive behavioral processes such as successive brightness discrimination (Stein & Kimble, 1966; Kimble, 1963).

Secondly, the corticals were considerably more deficient in acquisition of the task than normals. Analysis of the data indicated that the deficit was attributable to the cortically lesioned animals' inability to suppress responses on no-go trials.

Clearly, this study, rather than differentiating between the memory and response inhibition hypotheses, failed to

support either position. Rather than showing a retention deficit following hippocampal lesions as indicated by high latency ratios, the hippocampals were facilitated in the acquisition of low latency ratios as compared to both of the other groups. And rather than showing a response inhibition deficit, hippocampals were able to withhold responses on no-go trials significantly better than either of the other two groups. Furthermore, since the corticals were worse at suppressing responses on no-go trials than the other groups and hippocampals also had the same cortical area removed in their lesions, it might be assumed that the bilateral damage to the hippocampus actually facilitated behavioral suppression.

In a follow-up study, Walker et al. (1970) attempted to (1) confirm the above facilitated performance of hippocampal animals on the single-alternation go, no-go task at a 10-second ITI and (2) test the hypothesis that the facilitation was due to the hippocampal animals' ability to attend more to relevant cues and less to irrelevant cues than corticals or normals. The animals were trained to a low-level criterion (response and latency ratios less than 1.00 for two consecutive days) and then a S^D was introduced which consisted of a light coming on over the bar during go trials. It was expected that if the hippocampal animals were attending more to relevant than irrelevant cues than the other two groups, the removal of the S^D would disrupt the performance of the corticals and normals but not the hippocampals.

As in the previous study, the hippocampals acquired the task significantly better than the corticals or normals, as measured by the latency ratios; however, they were not significantly different from the normals on the response measure. This failure of the response ratio to indicate facilitation, as it did in the previous study, was attributed to the small n and the low-level criterion. The corticals were also significantly worse than the other two groups on the response ratios. This study essentially replicated the observations made in the previous study. However, neither the introduction nor the removal of the S^D differentially affected the response or latency ratios of the three groups.

In the last study of this series, Walker et al. (1972) studied the effect of increasing ITIs on performance of the single-alternation go, no-go task in hippocampal, cortical, and control animals. The previous literature concerning the effect of ITI length on performance in hippocampal animals has been inconsistant. For example, Liss (1968) found no deficit in both one-way active and passive avoidance tasks with an ITI of 35 seconds but a deficit in both tasks when the ITI was 10 minutes. On the other hand, both Jarrard and Lewis (1967) and Madsen and Kimble (1965) found rats to be equally impaired in the performance of a Lashley III maze at both a 10-second and a 10-minute ITI.

Rats were lesioned, allowed to recover, given magazine and CRF training, and then introduced to the go, no-go task

with a 10-second ITI (Walker et al., 1972). The length of the ITI was successively increased to 20, 40, and 80 seconds as the animals reached a criterion of three consecutive sessions at less than 0.50 on both latency and response ratios at each ITI.

Performance for all groups at the 10-second ITI was identical to that described in the first study (Means et al., 1970). There was no significant difference between groups at the 20-second ITI, but a progressive deficit in the performance of the hippocampal animals was observed at the 40- and 80-second ITIs. At the 40-second ITI, the hippocampals were significantly worse than the other two groups with no difference between the corticals and normals. Both corticals and hippocampals required significantly more sessions than normals to reach criterion at the 80-second ITI.

Those hippocampals that reached criterion at the 40-second ITI showed no improvement in either the latency or response measures during their 400 trials at the 80-second ITI. The deficit in the performance of the corticals was again due to their inability to withhold responses on the no-go trials. Since all animals reached criterion at the 20-second ITI, whenever an animal failed to reach criterion at the 40- or 80-second ITI, it was retested at the 20-second ITI. All animals retested at the 20-second ITI re-reached criterion with three to six sessions, suggesting that the deterioration of performance was due to the longer ITIs and not to some other variable.

The data of Walker et al. (1972) indicate that hippocampectomized rats can learn an alternation habit and further suggest the possibility that the information necessary for the solution of the alternation task is not capable of being held in immediate memory as long in hippocampal animals as it is in normals.

Distractability and Memory

The authors suggested that the perfromance deficit seen in the animal with hippocampal lesions at the longer ITIs might be due to the more rapid dissipation of the memory trace either spontaneously or through increased susceptability to disruption by distracting stimuli. They emphasized that if hippocampals are more distractable than normals, longer ITIs should increase the probability of their distraction and the resultant loss of memory for the events of the preceding trial.

This possibility is suggested by Milner's (1959) observation that the immediate memory of H. M. was very susceptible to disruption by attentional shifts. Furthermore, Douglas and Pribram (1966), in their model of limbic function, have postulated that the hippocampus protects memory consolidation from disruption by irrelevant or novel stimuli through an inhibitory gate acting on sensory input. Similarly, Kimble (1968) has suggested that the hippocampus has inhibitory control over the arousal systems of the lower brain through which it may mediate a process of internal inhibition. Kimble also suggests that this inhibitory

process might protect the process of memory consolidation from potential disruption by sensory input.

If these theories are correct, one might expect novel stimuli to be significantly more disrupting of memory formation in hippocampals than normals. Douglas and Pribram (1969) have demonstrated that hippocampals show a deficit in their ability to habituate the orienting response to novel stimuli. Such a deficit might easily result in increased distractability and loss of memory.

However, other researchers have found that hippocampal animals are less distractable than normals during the execution of prepotent responses or attentional processes. For example, hippocampals have been found to be less distractable than normals by novel stimuli introduced during performance in a straight-alley maze (Isaacson & Wickelgren, 1962; Riddel et al., 1969). Hendrickson et al. (1969) have shown that while hippocampals have no impairment in their abiltiy to orient per se, it is very difficult for them to orient to a novel stimulus presented subsequent to, but in the presence of, a previous stimulus.

In fact, a lack of distractability by hippocampally lesioned animals during attention or prepotent responding can be accounted for by Kimble's (1968) suggestion that the inhibitory properties of the hippocampus permit a decoupling of attention from irrelevant stimuli. In the absence of the hippocampus, once a stimulus has gained control of the

attentional system, it should be exceedingly difficult for the animal to shift its attention to a new stimulus, explaining why it is so difficult for hippocampal animals to perform reversals.

But the question now becomes, What effect do novel distracting stimuli have on learning and memory in hippocampal animals in the absence of confounding prepotent or attention responses? That is, hippocampals appear to be less distractable during their performance of prepotent responses, but may be more distractable than normals when they are not executing such responses as during an ITI. Unfortunately, the data bearing on this point are inconclusive. That increased distraction during ITIs might impair memory consolidation in normals is indicated by the fact that rats left in darkness during the ITI learn a horizontal-vertical discrimination more efficiently than those animals for whom the house lights were left on during the same period of time (Thompson, 1957). Also, Miller et al. (1969) have demonstrated that a blinking light interposed in the period between footshock and ECS following one-trial passive avoidance training produced significantly more amnesia than the absence of the photic stimulation.

Walker and Means (1972) have, in fact, found that interpolated task activity during ITIs was more disruptive of established single-alternation go, no-go performance in hippocampals than in normals. It was observed, however,

that with repeated presentation of the interpolated task, performance returned to the levels existing prior to introduction of the interpolated task, suggesting a habituation to the novel stimulation not predicted by the theories of Douglas (1967) and Kimble (1968).

In addition, Kimble and Pribram (1963) have shown that both hippocampal and control monkeys made fewer errors on visual discrimination tasks at longer (6 minutes) rather than shorter ITIs. Orbach et al. (1960) found no deficit in hippocampal monkeys in their acquisition of a simple visual discrimination habit with massed trials of an interpolated task during the ITIs.

However, in the tasks used in the latter two studies, cues for the discrimination of the correct response were present during every trial. In the single-alternation go, no-go task, no such cues are present on any trial to indicate a go or no-go response. Here performance depends upon maintaining the memory of the previous trial throughout the ITI.

A second problem with the distractability hypothesis is that if the deficit in performance seen in the hippocampals at the longer ITIs in the single-alternation go, no-go task is due to a loss of memory for the events occurring on the preceding trial, for whatever reason, why is there a deficit in the response ratio as well as the latency ratio. Presumably, if the animals had learned the alternation pattern

prior to being shifted to the 40- or 80-second ITI, even if they could not remember whether the trial was a go or no go (as indicated by the latency ratios), they would know which trial it was after their first response. In other words, if the only thing producing the performance deficit at the longer ITIs was disruption of the memory of the preceding trial, we would expect the deficit to be manifested only on the latency ratios.

In this regard Walker et al. (1972) have also mentioned the possibility that the performance deficit of the hippocampal animals at the longer ITIs might be due to frustration or confusion resulting from the inability to predict the consequences of the next trial. Such a frustration phenomenon working in conjunction with the disruption of memory during the ITI could account for the sustained performance deficit observed in the hippocampal animals.

Change in Conditions

While it is intriguing to think that the deficit seen at the longer ITIs is due to an impairment of short-term or immediate memory, an alternative explanation remains a possibility. As mentioned above, an early interpretation of the behavioral deficits produced by hippocampal lesions was that such lesions produce an impairment in response inhibition. The deficit is best observed as an inability to modify behavior in accordance with changes in experimental conditions. Most notable in this respect, are the numerous descriptions of impaired performance during reversal

training (Mahut & Cordeau, 1963; Thompson & Langer, 1963; Kimble & Kimble, 1965; Silveira & Kimble, 1968). More recently, Isaacson (1971) has postulated the necessity of an intact hippocampus if an animal is to be capable of suppressing on-going behavior in favor of new, more adaptive behavior hypotheses.

The study by Walker et al. (1972) employed successive changes if ITI length within the same animals. Their data indicate that each time the ITI was increased, a performance decrement was seen in the ratios, primarily due to an increase in no-go responses and a decrease in no-go latency. It is, therefore, quite possible that the performance deficit seen in this study is, at least in part, the result of the subjects' inability to adapt to the changes in the experimental conditions.

Inter-trial Interval

The present research was designed in response to both the inconsistency of the previous literature concerning the effect of both ITI length and alternation tasks on hippocampal animals and the desire to clarify the reason for the decreased performance by hippocampals on the single-alternation go, no-go task with longer ITIs. For example, as mentioned above, Liss (1968) found a long ITI (10 minutes) to be disruptive of both one-way active and passive avoidance while a short ITI (35 seconds) was not. In agreement with this, Walker et al. (1972) found the performance of hippocampally lesioned animals on a single-alternation go,

no-go task to be inversely related to the length of the ITI (10, 20, 40, and 80 seconds). However, Kimble and Pribram (1963) have shown hippocampal monkeys to perform a visual discrimination better at a longer ITI (6 minutes) than at a shorter ITI. And both Madsen and Kimble (1965) and Jarrard and Lewis (1967) found hippocampally lesioned rats to be equally impaired in the performance of a Lashley III maze at both long (10 minutes) and short (10 seconds) ITIs. This research can only be summarized by saying that the performance deficits seen at long or short ITIs in hippocampally lesioned animals are task specific.

Alternation

The data are even less clear concerning the effect of hippocampal lesions on the performance of alternation tasks. While hippocampectomized animals have no more difficulty learning a direct delayed response task at short ITIs (5-10 seconds) than normals (Orbach et al., 1960; Mahut & Cordeau, 1963), they are impaired on both original post-operative and retention learning of spatial delayed alternation with 5- to 10-second ITIs (Orback et al., 1960; Mahut & Cordeau, 1963; Pribram et al., 1962; Racine & Kimble, 1965) and superior to controls on acquisition of two-bar alternation (Jackson & Strong, 1969) and single-alternation (non-spatial) go, no-go tasks (Brown et al., 1969; Means et al., 1970; Walker et al., 1970, 1972) at short ITIs (10 seconds). Also, while hippocampal damage results in animals showing deficits in spontaneous alternation (Roberts

et al., 1962), the animals are capable of learning alternation responses, both spatial and temporal post-operatively (Jackson & Strong, 1969; Walker et al., 1972).

Walker et al. (1972) have also pointed out the discrepancy between the operant studies which show facilitated acquisition of an alternation habit following hippocampal lesions (Brown et al., 1969; Jackson & Strong, 1969; Means et al., 1970; Walker et al., 1970) and maze studies which produce deficits in both spatial and temporal alternation following hippocampal lesions (Racine & Kimble, 1965; Franchina & Brown, 1970; Means et al., 1970).

The results of these studies are very difficult to explain within a single theoretical framework. For example, a delayed alternation deficit might be due to one of two things: (1) loss of memory during delay or (2) response perseveration. Walker et al. (1972) suggest that deficits are seen in maze studies and not in operant studies because the former provide more opportunity for between-trial stimulation, such as experimenter handling, which may be more disruptive to hippocampally damaged animals than normals. This, however, does not fully explain the performance deficits seen in monkeys performing spatial delayed alternation in a WGTA at ITIs equivalent to or less than those used in the temporal alternation tasks in which hippocampal animals show facilitated acquisition (Orbach et al., 1960; Mahut & Cordeau, 1963; Pribram et al., 1962).

Likewise, the spatial perseveration argument does not explain why hippocampals are facilitated in two-bar alternation (Jackson & Strong, 1969).

Research Intent

Consequently, the intent of this research is two-fold. The first is to test the generality of the effects of hippocampal lesions on performance of the single-alternation go, no-go task by employing pre-operative training. In all three of the earlier studies by Means and Walker, subjects were trained post-operatively. In addition, other studies describing post-operative deficits in performance of tasks involving delayed spatial alternation (Orbach et al., 1960; Pribram et al., 1962) or delayed-matching-from-sample (Drachman & Ommaya, 1964) also report deficits in post-operative acquisition as well. The single-alternation go, no-go design, is a task on which hippocampal lesioned animals are known to show acquisition equal to or better than unoperated controls at short ITIs. Thus, pre-operative-training-post-operative testing should serve to demonstrate the generality of the lesion effect.

The pre-operative training and post-operative testing will also permit the second intent of this research which is to determine whether or not the deficits seen with the longer ITIs in the single-alternation go, no-go task (Walker et al., 1972) are due to either (1) a change in experimental conditions, (2) a lack of any transfer of learning from pre-operative to post-operative testing, or (3) a memory impairment.

There are essentially two components to the acquisition of a single-alternation task: (1) the acquisition of an alternation habit, which, following CRF training, consists primarily of learning to withhold responses on every other trial (go, no go) and (2) inter-trial memory. Once the alternation habit has been learned, performance on each trial is dependent upon the animal's remembering the events of the preceding trial throughout the ITI. The longer the ITI, the longer this information must be held in memory for successful performance. Hence, single alternation is particularly well suited to the study of short-term memory.

With pre-operative training, as employed in this study, the animals will have already acquired the alternation habit prior to post-operative testing. Post-operative performance would then be a function of the influence of brain surgery upon retention.

It is possible that post-training surgery could eliminate the alternation habit from the animals' behavioral repertoire. However, one intention of this study is to replicate, in so far as possible, the performance data derived from those studies using a surgery-test design (Means et al., 1970; Walker et al., 1970; Walker et al., 1972). If surgery destroys the alternation habit, reacquisition might be expected to look like original learning, post-operatively (surgery-test).

MATERIALS AND METHODS

Subjects

The subjects were male hooded rats of the Long-Evans strain, purchased from Blue Spruce Farms, Altamount, New York. The rats were approximately 200 gm. at the start of the experiment. They were individually housed and maintained on a 12-hour-light-12-hour-dark cycle.

Surgery and Histological Procedure

Thirty-six rats received bilateral brain lesions made by aspiration of the hippocampus and overlying cortex, 36 received bilateral lesions of only the cortex overlying the hippocampus, and 24 sham-operated controls were produced by opening the calvarium bilaterally. Surgery was performed under aseptic conditions employing essentially the same procedure as described by Isaacson, Douglas, and Moore (1961).

After completion of behavioral testing, operated animals were sacrificed with an overdose of chloroform and perfused with saline and Formalin. The brains were removed imbedded in celloidin, sectioned at 30 μ, and two series of every tenth section were mounted. One series was stained with thionin and the other series was stained by the Weil method.

Apparatus

All behavioral testing was done in three identical Lehigh Valley operant chambers and cubicles (No. 1417). Each chamber was equipped with two retractable levers on one end of the chamber (but the lever on the left side always remained retracted and was never used). The delivery port of a food magazine was centered between the levers. Associated with each chamber, was a Lehigh Valley pellet feeder (No. 1548) that delivered 45 mg. Noyes pellets.

Procedure

The rats were maintained at 85% of their ad-lib body weights throughout the experiment. One week after each rat had been reduced to 85% of its ad lib weight, magazine training was initiated. Beginning on the day following magazine training, each rat received a 10-minute CRF session daily until a total of 300 responses had been accumulated. During CRF training and subsequent go, no-go training, only the lever on the right side of the food magazine was used. The left lever was always retracted throughout the experiment. On the day following completion of the preliminary CRF training, all animals were given training on a single-alternation go, no-go task. Each session consisted of 20 discrete trials per day. Each trial consisted of a 20-second presentation of the lever followed by either a 10- or 50-second ITI during which the lever was retracted. On the

odd-numbered trials, the rats were reinforced (one 45-mg. Noyes pellet) for each response. On even-numbered trials, responses were not reinforced. No external cues were given. The maximum number of sessions permitted for any animal was 33.

The dependent variables were the latency to the first response and number of responses on each trial. The absolute latency and response scores were converted to latency and response ratios. The latency ratio for each animal is the total latencies to the first response on go trials/the total latencies to the first response on no-go trials for each session of 20 trials. The response ratio for each animal is the total responses on the no-go trials/total responses on go trials for each session of 20 trials. Latency and response ratios of less than 1.00 indicate fewer responses and a longer latency to respond on the non-reinforced no-go trials than on reinforced go trials. Thus, the smaller the latency and response ratios, the better the performance on the alternation task.

During pre-operative acquisition, 36 animals were trained on a 10-second ITI and 36 were trained on a 50-second ITI. All animals were trained to a criterion of three successive sessions with both latency and response ratios equal to or less than .40. The day after an animal reached criterion, it was given either bilateral hippocampal lesions, bilateral cortical lesions, or a sham operation.

Following a two-week post-operative recovery period, the animals were divided evenly into two larger groups (A and B) with half the animals in each of the three preceding lesion groups making up one of the two subsequent groups. Group A was then retested on a single-alternation go, no-go task with a 10-second ITI, while group B was retested on the same task with a 50-second ITI.

A second group of 24 animals was divided into two equal groups. One group received hippocampal lesions and the other received cortical lesions. Neither group had any training on the single-alternation task prior to surgery. Following surgery, one-half of each group was given acquisition training on the single-alternation task at a 10-second ITI and the other half at a 50-second ITI. This procedure produced four groups designated H-10, H-50, C-10, and C-50. Groups N-10 and N-50 were filled with the pre-operative performance data from animals in groups mentioned earlier in this study. Consequently, this research included a total of 18 groups which are summarized in Table 1 along with the actual number of animals in each group.

The data were analyzed in terms of latency and response ratios, sessions to criterion, difference scores, and per cent savings scores (pre-operative minus post-operative divided by pre-operative) for each group.

TABLE 1

SUMMARY OF EXPERIMENTAL GROUPS

Surgery											
Hippocampal				Cortical				Normal			
Pre-op. ITI		Post-op. ITI	n	Pre-op. ITI		Post-op. ITI	n	Pre-op. ITI		Post-op. ITI	n
10-H-10			5	10-C-10			6	10-N-10			5
10-H-50			5	10-C-50			5	10-N-50			5
50-H-10			7	50-C-10			6	50-N-10			6
50-H-50			7	50-C-50			6	50-N-50			6
H-10			6	C-10			7	N-10			34*
H-50			5	C-50			6	N-50			40*

*The data for groups N-10 and N-50 are the pre-operative performance of the animals in the other groups in this study.

RESULTS

Behavior

The mean data using combined latency and response ratios for each group are presented in Table 2. The mean data using independent latency and response ratios are presented in Table 3. Table 4 summarizes by lesion the mean group performance using combined ratios. Raw score data and group means for all subjects can be found in Appendix I and II.

An analysis of variance was performed on the difference scores between pre-operative and post-operative acquisition for the animals trained pre-operatively on the 50-second (pre-operative 10) and the 50-second (pre-operative 50) ITIs. The analysis revealed a significant ITI effect ($p < .05$) but no significant lesion effect for the pre-operative 10 group and a significant lesion effect ($p < .05$) but no ITI effect for the pre-operative 50 group.

As can be seen from Table 2, the animals in the 10-H-10 group revealed a dramatic negative savings post-operatively (-41.94%). Both the 10-C-10 and the 10-N-10 groups had a positive savings, with the corticals (35.02%) performing significantly better ($p < .05$) than the shams (3.24%). All groups trained at a 10-second ITI but trained post-operatively

at a 50-second ITI showed negative savings. In all six pre-operative 50 groups only the two hippocampal groups had negative savings. In addition there was no significant difference between the H-10 and N-10 groups, and the mean sessions to criterion for the H-10 (18.83) group in this study was higher than the mean for the H-10 (11.57) group in the previous study (Walker et al., 1972).

A differential analysis of the latency and response ratios, as described in Table 3, for the 10-H-10 group indicates that the entire post-operative deficit in that group was due to the response measure. The 10-C-10 group showed savings on both latency and response ratios; however, there was about twice as much savings on the response ratios as on the latency ratios. The 10-N-10 group indicated practically no savings on the latency measure with about 50% savings on the response measure. All groups trained pre-operatively at a 10-second ITI and changed post-operatively to a 50-second ITI had negative savings on both the latency and response ratios. Practically all of the pre-operative 50 groups except the two hippocampal groups had positive savings on both latency and response ratios. The exception was the response ratio for the 50-N-10 group which showed a slight negative savings (-5.43%). Both of the pre-operative 50 hippocampal groups showed negative savings on both the latency and response ratios.

The remainder of the data in this experiment consists of a large number of group comparisons for the purpose of

attempting to determine the nature of the performance deficit seen in hippocampally lesioned animals at long ITIs (Walker et al., 1972). Because these comparisons require extensive explanations which are best done in the Discussion section, the data in the form of these group comparisons are only summarized here in Table 5. All individual group comparisons were by the use of Student's t distribution upon both the difference scores (the difference between the number of sessions to criterion pre-operatively and post-operatively transformed by adding 25 to each raw score in order to eliminate negative numbers and the number of sessions to criterion on post-operative acquisition alone, whenever appropriate. While the Student's t test performed upon the two sets of data for each group comparison always produced a slightly different score, in no group comparison did one t score produce a significant difference when the other did not.

Histology

While there was variation in the size of the hippocampal lesions between animals, all hippocampal groups contained animals with lesions of comparable size, and performance was not related to the variation in the size of the lesions.

The four photomicrographs in Figure 1 are posterior-anterior sections through the brain of animal 9 (50-H-50) and are representative of the larger hippocampal lesions in the study. Figure 2 contains similar sections from animal 16 (50-H-50) and are representative of the smaller lesions.

In most of the hippocampal animals, the ventral lesion did not extend below the rhinal fissure. All of the hippocampal lesions included bilateral section of the fimbria. Of the 35 animals in this study, the stria terminalis was damaged unilaterally in five animals and bilaterally in five animals. The entorhinal cortex was also damaged in five animals unilaterally and in four animals bilaterally. In addition, 11 animals sustained slight unilateral damage to the thalamus, primarily to the lateral geniculate nucleus and one animal suffered rather extensive bilateral thalamic damage. Again, no correlation was observed between the number of sessions to criterion, on either the latency or response ratios, and any of the extra-hippocampal damage just described. In fact, the animal with the severe bilateral thalamic damage achieved criterion post-operatively in fewer sessions than the mean post-operative sessions to criterion for its group (50-H-50). Almost all of the animals showed evidence of bilateral thalamic nucleus degeneration.

Cortical lesions were primarily limited to the dorsolateral cortex overlying the hippocampus. In only 7 of 36 cortical animals did the lesion extend down to the rhinal fissure. Seven animals sustained very slight unilateral damage to the hippocampus, which was not related to performance. Figure 3 shows sections from animal 38 (10-C-50) which are representative of the larger cortical lesions, while Figure 4 contains sections from animal 41 (50-C-50) which are representative of the smaller cortical lesions.

TABLE 2

MEAN SESSIONS TO CRITERION: COMBINED RATIOS

Group	n	Latency and response ratios: Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		Pre-operative 10-sec. ITI			
10-H-10	5	8.80	12.60	-3.80	-41.94
10-C-10	6	15.00	7.50	7.50	35.02
10-N-10	5	11.20	9.40	1.80	3.24
10-H-50	5	15.40	23.40	-8.00	-39.46
10-C-50	5	11.00	18.00	-7.00	-79.62
10-N-50	5	11.20	16.20	-5.00	-41.54
		Pre-operative 50-sec. ITI			
50-H-10	7	15.42	17.28	-1.86	-35.60
50-C-10	6	17.83	8.71	7.83	35.12
50-N-10	6	18.33	14.50	2.17	14.68
50-H-50	7	17.71	19.85	-2.14	-11.03
50-C-50	6	17.00	7.66	9.33	50.82
50-N-50	6	18.00	3.33	14.67	80.17
		Post-operative 10-sec. ITI			
H-10	6		2.05		
C-10	7		19.14		
N-10	34		14.00		
		Post-operative 50-sec. ITI			
H-50	5		30.20		
C-50	6		24.83		
N-50	40		17.22		

TABLE 3

MEAN SESSIONS TO CRITERION: INDEPENDENT RATIOS

Group	n	Latency ratios: Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		Pre-operative 10-sec. ITI			
10-H-10	5	9.40	6.00	3.40	36.38
10-C-10	6	12.66	8.00	7.50	26.12
10-N-10	5	9.80	9.00	0.80	- 0.94
10-H-50	5	10.60	21.20	-10.60	-94.28
10-C-50	5	9.80	17.40	7.60	-86.24
10-N-50	5	10.00	10.20	- 0.20	- 6.64
		Pre-operative 50-sec. ITI			
50-H-10	7	15.00	14.44	0.57	-14.53
50-C-10	6	17.83	10.00	7.83	34.38
50-N-10	6	16.66	14.50	2.17	14.68
50-H-50	7	17.42	17.85	- 0.43	- 6.57
50-C-50	6	15.50	7.66	7.83	46.97
50-N-50	6	13.82	6.00	11.67	73.02
		Post-operative 10-sec. ITI			
H-10	6		15.83		
C-10	7		16.57		
N-10	34		10.38		
		Post-operative 50-sec. ITI			
H-50	5		26.40		
C-50	6		23.16		
N-50	40		16.04		

TABLE 3--(extended)

Response ratios			
Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
9.20	12.60	- 3.40	-37.08
13.16	6.00	7.17	41.45
11.00	5.40	5.60	47.62
15.20	22.80	- 7.60	-45.12
10.80	15.80	- 5.00	-60.56
10.20	14.20	- 3.40	-27.28
12.75	17.28	- 5.17	-71.81
14.50	8.83	5.67	37.55
12.83	12.16	0.67	- 5.43
12.42	18.42	- 6.00	-54.11
18.33	6.33	10.33	61.13
16.33	3.33	13.00	76.52
	16.66		
	18.24		
	11.59		
	28.8		
	18.0		
	14.53		

TABLE 4

MEAN SESSIONS TO CRITERION BY LESION: COMBINED RATIOS

Group	n	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
			Hippocampal		
10-H-10	5	8.80	12.60	- 3.80	-41.94
10-H-50	5	15.40	23.40	- 8.00	-39.46
50-H-10	7	15.42	17.28	- 1.86	-35.60
50-H-50	7	17.71	19.85	- 2.14	-11.03
H-10	6	--	20.50	--	--
H-50	5	--	30.20	--	--
			Corticals		
10-C-10	6	15.00	7.50	7.50	35.02
10-C-50	5	11.00	18.00	- 7.00	-79.62
50-C-10	6	17.83	8.71	7.83	35.12
50-C-50	6	17.00	7.66	9.33	50.82
C-10	7	--	19.14	--	--
C-50	6	--	24.83	--	--
			Normals		
10-N-10	5	11.20	9.40	1.80	3.24
10-N-50	5	11.20	16.20	- 5.00	-41.54
50-N-10	6	18.33	14.50	2.17	14.68
50-N-50	6	18.00	3.33	14.67	80.17
N-10	34	--	14.00	--	--
N-50	40	--	17.22	--	--

TABLE 5

OBSERVED SUPPORT FOR PREDICTIONS DIFFERENTIATING THREE HYPOTHESES CONCERNING THE DEFICIT IN THE PERFORMANCE OF SINGLE-ALTERNATION GO, NO GO FOLLOWING HIPPOCAMPAL LESIONS

Support for hypotheses	Observed Yes	Observed No
Change of conditions		
Differentiates change of conditions from memory disruption and lack of transfer.		
1. 50-H-10 significantly worse than H-10.		X
2. 10-H-50 significantly worse than H-50.		X
3. No significant difference between 50-H-10 and 10-H-50, both showing a deficit (10-H-50 may be slightly worse due to increased difficulty of the 50-second ITI task).	X	
Differentiates change of conditions from memory disruption but not lack of transfer.		
4. No significant difference between 50-H-50 and 50-N-50.		X
5. 10-H-50 significantly worse than 50-H-50.		X
6. 50-H-10 significantly worse than 10-H-10.		X
7. 50-H-10 significantly worse than 50-N-10.		X
Differentiates change of conditions from lack of transfer but not memory disruption.		
8. 10-H-50 significantly worse than N-50.	X	
9. 50-H-10 significantly worse than N-10.		X
Memory disruption		
Differentiates memory disruption from change of conditions and lack of transfer.		
1. No significant difference between 10-H-50 and 50-H-50, both showing negative savings.	X	
2. No significant difference between 50-H-10 and 10-H-10.	X	
3. No significant difference between 50-H-10 and 50-N-10.	X	
4. 50-H-50 significantly worse than 50-N-50.	X	
5. A significant difference between H-10 and H-50 as compared to the difference between N-10 and N-50.	X	
Differentiates memory disruption from change of conditions but not lack of transfer.		

TABLE 5--(continued)

Support for hypotheses	Observed Yes	Observed No
(Same as those that differentiate change of conditions from memory disruption and lack of transfer.)		
Differentiates memory disruption from lack of transfer but not change of conditions.		
8. 10-H-50 significantly worse than 10-N-50.		X
9. 10-H-50 significantly worse than N-50.	X	
Lack of transfer		
Differentiates lack of transfer from change of conditions and memory disruption.		
1. No significant difference between 10-H-50 and 10-N-50.	X	
2. No significant difference between 10-H-50 and N-50.		X
Differentiates lack of transfer from change of conditions but not memory disruption.		
(Same as those that differentiate change of conditions from both memory disruption and lack of transfer.)		
Differentiates lack of transfer from memory disruption but not change of conditions.		
(Same as those that differentiate memory disruption from both lack of transfer and change of conditions.)		

Figure 1. Posterior-anterior sections through the brain of animal 9 (50-H-50). The sections are representative of the larger hippocampal lesions in this study.

Figure 2. Posterior-anterior sections through the brain of animal 16 (50-H-50). The sections are representative of the smaller hippocampal lesions in this study.

Figure 3. Posterior-anterior sections through the brain of animal 38 (10-C-50). The sections are representative of the larger cortical lesions in this study.

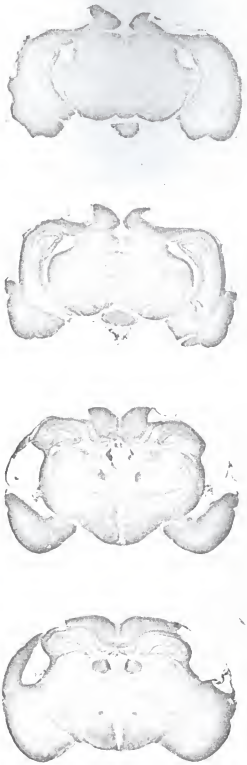
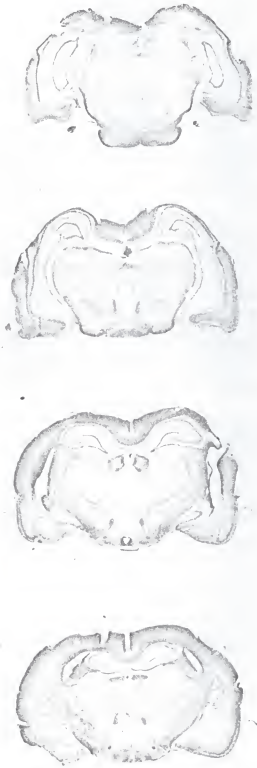


Figure 4. Posterior-anterior sections through the brain of animal 41 (50-C-50). The sections are representative of the smaller cortical lesions in this study.



DISCUSSION

The failure of the analysis of variance to reveal any discernible lesion effect in the animals trained pre-operatively at the 10-second ITI, even though both the 10-H-10 and the 10-H-50 animals demonstrated rather pronounced negative savings, is undoubtedly due to the fact that the 10-C-50 and the 10-N-50 animals also had large negative savings. Similarly, the fact that the pre-operative 50 corticals and normals in both the 10- and 50-second post-operative ITI groups showed positive savings while both the 50-H-10 and the 50-H-50 animals showed negative savings accounts for the significant lesion effect in the pre-operative 50 group. Consequently, in this experimental design, whether there is a lesion effect or an ITI effect appears to be a function of the length of the pre-operative ITI, with the shorter pre-operative ITI producing the ITI effect and the longer pre-operative ITI resulting in a lesion effect.

The negative savings in the 10-H-10 group is interesting because, while one might expect little or no savings due to the effect of radical surgery on the integration of the brain, because of the previous literature describing a rather consistent facilitated acquistion in

hippocampal animals trained post-operatively at a 10-second ITI, it would seem more probable that there would be a more rapid reacquisition of the task in the 10-H-10 group than in the 10-C-10 or 10-N-10 groups. However, a comparison of just the post-operative acquisition mean for the 10-H-10 group with the post-operative acquisition mean for the H-10 animals in the previous study (Walker et al., 1972) reveals that they are almost identical (12.6 and 11.57, respectively). Apparently, the negative savings score for the 10-H-10 group is due to the lower mean for pre-operative acquistion (8.8).

One would further expect, on the basis of the previous literature, that the 10-N-10 group would show considerable savings rather than practically no savings at all and that the 10-C-10 group would have the poorest performance, post-operatively, of the three groups rather than the best.

It is possible that the post-operative deficit seen in the 10-H-10 groups as compared to the facilitated acquisition of the H-10 animals in the earlier studies is due to the more stringent criterion used in this study. For example, Walker et al. (1972) used a criterion of three successive sessions with both latency and response ratios less than .50. This study required a criterion of three successive sessions with both latency and response ratios equal to or less than .40.

With respect to the cortical animals, it is possible that the lack of a post-operative performance deficit in the

10-C-10 group, as compared to the C-10 groups in the previous study (Walker et al., 1972), is the result of lesion differences between the two studies. In the earlier study, the cortical lesions were more lateral and ventral extending below the rhinal fissure. In the present study, only 19% of the cortical animals had lesions reaching the rhinal fissure.

The failure of the H-10 group to acquire the single-alternation task significantly faster than the N-10 group is also contrary to the earlier studies. The animals in this study demonstrated a greater degree of performance variability than those in the previous studies, and it is possible that a larger n in the H-10 group would have provided statistical significance. However, a look at the post-operative acquisition means for these two groups (Table 2) reveals that the H-10 group took more rather than fewer sessions (20.5) to reach criterion than the N-10 group (14).

A differential analysis of the latency and response ratios for the 10-H-10 group shows that the entire deficit produced in that group was due to the response measure. The 10-C-10 group showed savings on both latency and response ratios; however, there was about twice as much savings on the response ratios as on the latency ratios. The fact that the 10-C-10 animals showed positive savings, especially in the response ratios, is inconsistent with the earlier studies in which the deficit in the cortical group at the

10-second ITI was due entirely to a poor performance on the response ratios. The normals showed practically no savings on the latency measure with about 50% savings on the response measure.

Various group comparisons were made in an effort to determine if the performance deficit seen in hippocampally lesioned animals at longer ITIs on the single-alternation go, no-go task is due to the inability of hippocampal animals (1) to modify their behavior appropriately in response to a change in experimental conditions, (2) to transfer preoperative learning to the post-operative task, or (3) to hold the events of the preceding trial in memory as long as normals. Table 5 describes the predicted results of group comparisons that would differentiate each of the three hypotheses and whether or not the predicted relationships were actually observed in this research. The predictions made under each of the three hypotheses differentiate a given hypothesis from one or both of the other two.

Change-of-Conditions Hypothesis

Group comparison predictions 1 through 3 made under the change-of-conditions hypothesis in Table 5 differentiate that hypothesis from both the memory disruption and lack-of-transfer hypothesis. Predictions 4 and 7 differentiate the change-of-conditions hypothesis from memory disruption but not from the lack-or-transfer hypothesis, and predictions

8 and 9 differentiate the change-of-conditions hypothesis from the lack-of-transfer hypothesis but not from memory disruption.

Only one of the three predictions differentiating the change-of-conditions hypothesis from the other two was statistically significant ($p < .05$).

There are several other observations which contra-indicate a change-of-conditions hypothesis as an explanation for the performance deficit seen in hippocampal animals at longer ITIs (Walker et al., 1972). First, in the study by Walker et al. (1972), several of the hippocampal animals were never able to perform the single-alternation task at the longer ITIs (40 and 80 seconds). While the change from one ITI to another was disruptive, it was not prohibitive at the shorter ITIs since all hippocampals reached criterion at the 20-second ITI and approximately half achieved criterion at the 40-second ITI. Why then did none of the hippocampals reach criterion at the 80-second ITI? In other words, while a change of conditions should initially disrupt performance, if an inability to modify behavior in response to a change in experimental conditions is the only thing affecting the performance of hippocampal animals, then there is no obvious reason why it should have a permanently disrupting effect at one ITI but not at another.

Also in the Walker et al. (1972) study, hippocampally lesioned animals were changed from the 80- or 40-second ITI back to the 20-second ITI without any noticeable disruption.

Even if the animals did not reach criterion at the 40- or 80-second ITI, they were still capable of performing the alternation habit, reachieving criterion on the 20-second ITI task within three to six sessions.

Secondly, both the 10-H-10 and the 50-H-50 groups demonstrated negative savings (-41.94% and -11.03%, respectively) as compared to the 10-C-10 (35.02%), 10-N-10 (3.24%), 50-C50 (50.82%), and 50-N-50 (80.17%) groups. Since there is no change in the length of the ITI between pre- and post-operative testing in these groups, the change-of-conditions hypothesis is unable to account for the negative savings in the hippocampal animals.

Thirdly, while the 10-H-50 animals did show a negative savings (-39.46%) as would be predicted by the change-of-conditions hypothesis, it was almost identical to the negative savings seen in the 10-H-10 (-41.94%).

And fourthly, the 10-C-50 (-79.62%) and the 10-N-50 (-41.54%) groups also had negative savings not statistically different from that of the 10-H-50 (-39.46%) animals. That is, all three groups (10-H-50, 10-C-50, and 10-N-50) were adversely affected by the change from a 10-second pre-operative ITI to a 50-second post-operative ITI. Again, this was indicated in the overall analysis of variance as the ITI effect for the pre-operative 10 groups.

The data for the pre-operative 50 groups are more supportive of the change-of-conditions hypothesis as suggested by

the analysis of variance lesion effect for this group. For example, the 50-H-10 group had negative savings (-35.6%) as compared to the 50-C-10 (35.12%) and the 50-N-10 (14.68%) groups. However, the 50-H-50 group also contributed to the lesion effect as it too had negative savings (-11.03%) significantly different from the 50-C-50 (50.82%) and the 50-N-50 (80.17%) groups ($p < .05$). This latter observation is not predicted by the change-of-conditions hypothesis.

That there is no significant difference between the 50-H-10 and 10-H-50 groups, with both showing a deficit, is a major prediction by the change-of-conditions hypothesis and supported by this study. However, its value as support for a change-of-conditions explanation for the performance deficit seen in hippocampal animals at the longer ITIs (walker et al., 1972) is weakened by the fact that corticals and normals as well as hippocampals demonstrated negative savings when changed from a pre-operative 10-second ITI to a post-operative 50-second ITI.

The change-of-conditions hypothesis is, however, supported by the pre-operative 50 groups which show that the 50-H-10 animals have negative savings (-35.6%) as compared to the 50-C-10 (35.12%) and 50-N-10 (14.68%) animals. In other words, a change-of-conditions phenomenon appears to be operating when the change is from a 50-second pre-operative ITI to a 10-second post-operative ITI but not when

the change-of-conditions is from a 10-second pre-operative ITI to a 50-second post-operative ITI.

All four of the predictions that differentiated the change-of-conditions hypothesis from the memory but not the transfer hypothesis failed to be supported by this research. Since the change-of conditions and memory hypotheses predict different things in these comparisons, they suggest that memory disruption may be at least contributing to the performance of the hippocampally lesioned animals.

Memory Disruption Hypothesis

All five of the predictions that differentiate the memory disruption hypothesis from the other two hypotheses were supported by this research. It is, in fact, the only set of predictions differentiating a given hypothesis from the other two that received 100% support.

The fact that there was no significant difference between the 10-H-50 and the 10-N-50 groups is, however, contrary to the prediction of the memory hypothesis. This lack of significant difference might be accounted for by the ITI effect found in the pre-operative 10 groups.

Because the 10-H-10 group (-41.94%) was approximately four times worse, in terms of savings scores, than the 50-H-50 group (-11.03%)--another observation opposite to that predicted by the memory hypothesis--it would appear that the test-surgery-test paradigm using a single-alternation go, no-go task does not have the same effect on rats as

the surgery-test design used by Walker et al. (1972). This is in agreement with other research describing post-operative deficits in performance of tasks involving delayed spatial alternation (Orbach et al., 1960; Pribram et al., 1962) or delayed matching from sample (Drachman & Ommaya, 1964). Also, Thomas (1971) pre-operatively trained rats on a four-unit multiple-U maze. While there was a wide range of variability, as a group, the rats showed negative savings (-22%) following bilateral hippocampal lesions.

However, pre-operative training does not always produce a disruption of performance in hippocampally lesioned animals. For example Traux and Thompson (1969) pre-operatively trained rats on a simultaneous white-gray discrimination. Following extensive bilateral hippocampal lesions, retention of the visual habit was excellent as indicated by error savings scores exceeding 75%. Also, Buerger (1970) has found cats perform a successive (go, no-go) auditory-brightness discrimination better after hippocampal lesions if they first had pre-operative training on the same task.

It is possible that the 10-H-10 animals demonstrated a greater deficit than the 50-H-50 animals post-operatively, because of over-learning occurring in the latter group. While the means of the pre-operative acquisition scores for the above two groups were not statistically significant (14 sessions for the 10-second ITI and 17.2 sessions for the

50-second ITI), it did take the animals more sessions to learn the alternation task with the 50-second ITI than with the 10-second ITI. Furthermore, there was a statistical significance between the post-operative acquisition scores for the 10-N-10 and the 50-N-50 groups ($p < .05$), with the 50-N-50 group having a savings of 80.17% and the 10-N-10 group a savings of 14.68%.

It is also possible that the failure to see a significant difference between the 10-H-10 and the 50-H-50 groups, or any of the other groups, was the result of a ceiling effect produced by the 33-session cutoff employed in this experiment. Table 6 lists the number of animals in each of the hippocampal groups that did not reach criterion within the 33 sessions along with the group mean latency and response ratios for the thirty-third session alone. As can be seen by Table 6, all animals in the 10-H-10 group reached criterion while two in the 50-H-50 group did not. Table 7 lists the mean latency and response ratios on the thirty-third session alone for each hippocampal animal not achieving criterion.

However, as can also be seen by Table 6, the greatest number of animals not reaching criterion in any one group was three. By raising the number of sessions permitted in this experiment, it is possible that a group might be made significantly different from another because of the scores of only one or two animals. Rather than increasing the

number of sessions, increasing the number of subjects in each group would have been preferable.

In addition, it is interesting that Table 6 also indicates that for those hippocampal animals not achieving criterion, the response ratios for the last session are approximately double the latency ratios. A differential analysis of the group mean latency and response ratios to criterion indicates that all hippocampal groups, except the 10-H-10 group, had negative savings on both latency and response ratios. Group 10-H-10 had negative savings on only the response measure. However, there was no significant difference between the mean number of latency and response ratios to criterion within any of the hippocampal groups.

While the data are not conclusive, then, there is evidence that memory disruption does influence the performance of hippocampally lesioned animals at long (50-second) ITIs on a single-alternation go, no-go task.

Lack-of-Transfer Hypothesis

Only one of the two predictions that differentiate the lack-of-transfer hypothesis from the other two hypotheses was supported by this research; i.e., no significant difference was observed between the 10-H-50 and the 10-N-50 animals. However, this result might also be due to the ITI effect described previously for the pre-operative 10 groups.

Furthermore, the lack-of-transfer hypothesis would predict no difference between the post-operative acquisition

scores of the 10-H-10 animals and the H-10 animals. There is, in fact, a significant difference between these two groups ($p < .05$). The lack-of-transfer hypothesis would also predict a zero savings in the 10-H-10 animals, while this study revealed a -35.6% savings. There is, thus, little evidence that the hippocampal lesions are causing the post-operative tasks to be treated just as if they were new tasks.

It should be reemphasized that there are several differences between the present study and the earlier study by Walker et al. (1972). (1) Unlike in the previous study, rats were trained pre-operatively. As indicated by the overall analysis of variance, this procedure had a differential effect on performance depending upon the ITI of the pre-operative training. (2) Cortical lesions were more dorsal in this study than in the previous study. This might have accounted for the failure to see performance deficits in the cortical groups other than the 10-C-50 group. (3) Lastly, the longest ITI used in this study was 50 seconds, while the longest used by Walker et al. (1972) was 80 seconds. This may have resulted in the failure to see significant differences between animals trained post-operatively at the 10- and 50-second ITIs.

Finally, it is fairly evident, as a result of the rather large variability between subjects within the same experimental groups, that much larger n's would make the

data of this experiment more reliable. The data also suggest that any one of the three hypotheses studied in this experiment cannot fully explain the behavior of hippocampal animals during their performance of a single-alternation go, no-go task.

TABLE 6

NUMBER OF HIPPOCAMPAL ANIMALS NOT REACHING CRITERION AND GROUP MEAN RATIO SCORES FOR THE THIRTY-THIRD SESSION

Group	Group n	Number not reaching criterion	Mean latency ratio	Mean response ratio
10-H-10	5	0	--	--
10-H-50	5	3	0.73	2.13
50-H-10	7	1	0.53	0.51
50-H-50	7	2	0.64	1.58
H-10	6	1	0.53	0.59
H-50	5	3	0.58	1.08

TABLE 7

HIPPOCAMPAL ANIMALS NOT REACHING CRITERION
AND THEIR MEAN RATIO SCORES ON
THE THIRTY-THIRD SESSION

Animal	Mean latency ratio	Mean response ratio
	10-H-50	
26	0.32	0.90
49	1.15	4.03
28	0.72	1.45
ΣX	2.19	6.38
$\bar{X}$	0.73	2.13
	50-H-10	
9	0.53	0.51
	50-H-50	
8	0.62	1.73
24	1.29	3.01
ΣX	1.91	4.74
$\bar{X}$	0.64	1.58
	H-10	
22	0.53	0.59
	H-50	
9	0.68	0.58
10	0.55	2.07
31	0.51	0.59
ΣX	1.74	3.24
$\bar{X}$	0.58	1.08

SUMMARY

Rats were given pre-operative training on a single-alternation go, no-go task at either a 10- or 50-second ITI, given either bilateral hippocampal or cortical lesions or a sham operation, and post-operatively trained at either a 10- or 50-second ITI on the single-alternation go, no-go task. The results are summarized as follows:

1. This research was not successful in replicating the facilitated acquisition of the hippocampal animals or the performance deficit of the cortical animals observed in previous studies (Means et al., 1970; Walker et al., 1970, 1972).
2. Negative savings scores in hippocampal animals trained pre-operatively and post-operatively at the same ITI suggest that the hippocampal lesions made after training influence post-operative learning differently from post-operative learning without pre-operative training.
3. Changing the ITI from 10 seconds pre-operatively to 50 seconds post-operatively appears to affect all animals (hippocampals, corticals, and normals) adversely, producing negative savings, while the change from 50 seconds pre-operatively to 10 seconds post-operatively affects only the hippocampals adversely.

4. Finally, while the data provided by the group comparisons were by no means conclusive, they did indicate that memory disruption is the most tenable of the three hypotheses for explaining the performance deficit seen in hippocampally lesioned animals at longer ITI's on the single-alternation go, no-go task.

APPENDIX I

RAW SCORE SESSIONS TO CRITERION: COMBINED RATIOS

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		10-H-10		
39_1	6	6	0	0
21_1	11	4	7	63.6
45_2	8	12	- 4	- 50.0
43_2	9	12	- 3	- 33.3
32_2	10	29	-19	-190.0
ΣX	44	63	-19	-209.7
$\bar{X}$	8.8	12.6	-3.80	-41.94
		10-C-10		
25_1	9	3	6	66.6
27_1	8	12	- 4	- 50.0
12_1	16	5	11	68.7
30_2	11	12	- 1	- 9.1
41_2	15	7	8	53.3
31_2	31	6	25	80.6
ΣX	90	45	45	210.1
$\bar{X}$	15	7.5	7.50	35.02
		10-N-10		
4_1	10	17	- 7	- 70
22_1	7	13	- 6	- 85.7
29_1	12	5	7	58.3
46_2	11	4	7	63.6
37_2	16	8	8	50.0
ΣX	56	47	9	16.2
$\bar{X}$	11.2	9.4	1.80	3.24

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		10-H-50		
13_1	12	10	2	16.6
15_1	9	8	1	11.1
26_1	22	33	-11	- 50.0
49_2	12	33	-21	-125.0
28_2	22	33	-11	- 50.0
ΣX	77	117	-40	-197.3
$\bar{X}$	15.4	23.4	-8.0	-39.46
		10-C-50		
19_1	7	17	-10	-142.8
14_1	11	8	3	27.2
36_2	10	22	-12	-120.0
34_2	16	10	6	37.5
38_2	11	33	-22	-200.0
ΣX	55	90	-35	-398.1
$\bar{X}$	11	18	-7	-79.62
		10-N-50		
34_1	7	11		- 57.1
43_1	9	13		- 44.4
38_1	12	9		25.0
42_2	12	15		- 25.0
47_2	16	33		-106.2
ΣX	56	81		-207.7
$\bar{X}$	11.2	16.2		-41.54

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		50-H-10		
6_1	11	17	- 6	- 54.2
5_1	18	8	10	55.5
7_2	9	21	-12	-133.3
13_2	16	15	1	6.2
19_2	23	18	5	21.6
17_2	20	9	11	55.0
9_2	11	33	-22	-200.0
ΣX	108	121	-13	-249.2
$\bar{X}$	15.43	17.28	-1.86	-35.60
		50-C-10		
35_1	12	7	5	41.6
37_1	29	5	24	86.2
23_1	13	13	0	0.0
22_2	17	8	9	53.9
4_2	13	16	- 3	- 23.1
1_2	23	11	12	52.1
ΣX	107	61	47	210.7
$\bar{X}$	17.83	10.17	7.83	35.12
		50-N-10		
11_1	14	17	- 3	- 21.4
18_1	12	5	7	58.3
23_2	16	7	9	56.2
12_2	19	16	3	15.7
16_2	16	20	- 4	- 25.0
5_2	23	22	1	4.3
ΣX	110	87	13	88.1
$\bar{X}$	18.33	14.5	2.17	14.68

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		50-H-50		
36_1	12	17	- 5	- 25.0
16_1	13	7	6	46.1
9_1	25	17	8	32.0
20_2	11	17	- 6	- 54.5
14_2	16	15	1	6.2
24_2	22	33	-11	- 50.0
8_2	25	33	- 8	- 32.0
ΣX	124	139	-15	- 77.2
$\bar{X}$	17.71	19.86	-2.14	-11.03
		50-C-50		
41_1	11	9	2	18.1
20_1	16	13	3	18.7
10_1	18	10	8	44.4
21_2	15	5	10	66.6
10_2	19	4	15	78.9
2_2	23	5	18	78.2
ΣX	102	46	56	304.9
$\bar{X}$	17	7.67	9.33	50.82
		50-N-50		
31_1	12	3	9	75.0
7_1	15	5	10	66.6
40_1	22	3	19	86.3
18_2	16	3	13	81.2
3_2	20	3	17	85.0
6_2	23	3	20	86.9
ΣX	108	20	88	481.0
$\bar{X}$	18	3.33	14.67	80.17

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
		H-10		
5_2		8		
3_2		21		
7_2		15		
18_2		25		
21_2		11		
22_2		33		
ΣX		123		
$\bar{X}$		18.83		
		C-10		
2_2		33		
4_2		33		
6_2		14		
8_2		12		
16_2		13		
20_2		16		
24_2		12		
ΣX		133		
$\bar{X}$		20.43		
		N-10		
39_1		6		
19_1		7		
22_1		7		
34_1		7		
27_1		8		
15_1		9		
25_1		9		
43_1		9		

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
4_1		10		
14_1		11		
21_1		11		
13_1		12		
29_1		12		
38_1		12		
12_1		16		
26_1		22		
8_1		27		
45_2		8		
36_2		10		
32_2		10		
30_2		11		
38_2		11		
46_2		11		
42_2		12		
43_2		12		
49_2		12		
41_2		15		
34_2		16		
37_2		16		
47_2		16		
28_2		22		
31_2		31		
33_2		33		
40_2		33		
ΣX		474		
$\bar{X}$		14		
		H-50		
9_2		33		
10_2		33		

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
17_2		23		
31_2		33		
25_2		29		
ΣX		151		
$\bar{X}$		30.2		
		C-50		
11_2		33		
14_2		12		
15_2		14		
27_2		33		
28_2		33		
29_2		24		
ΣX		149		
$\bar{X}$		24.83		
		N-50		
6_1		11		
41_1		11		
18_1		12		
31_1		12		
35_1		12		
36_1		12		
16_1		13		
23_1		13		
11_1		14		
7_1		15		
20_1		16		
32_1		17		
5_1		18		
10_1		18		

Animal number	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
40_1		22		
33_1		22		
37_1		29		
9_1		25		
7_2		9		
23_2		16		
9_2		11		
20_2		11		
4_2		13		
21_2		15		
16_2		16		
18_2		16		
13_2		16		
14_2		16		
22_2		17		
10_2		19		
3_2		20		
12_2		20		
17_2		20		
24_2		22		
1_2		33		
2_2		23		
5_2		23		
6_2		23		
19_2		23		
8_2		25		
ΣX		689		
$\bar{X}$		17.22		

Note: Due to the large number of animals used in this experiment, it was necessary to run them in two replications. The animal number subscripts indicate to which replication the animal belonged.

APPENDIX II

RAW SCORE SESSIONS TO CRITERION: INDEPENDENT RATIOS

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				10-H-10				
39_1	6	4	2	33.3	6	6	0	0
21_1	11	4	7	63.6	11	4	7	63.6
45_2	8	6	2	25.0	8	12	- 4	- 50.0
43_2	12	12	0	0	11	12	- 1	- 9.0
32_2	10	4	6	60.0	10	29	-19	- 19.00
ΣX	47	30	17	181.9	46	63	-17	-185.4
$\bar{X}$	9.4	6	3.40	36.38	9.2	12.6	-3.40	- 37.08
				10-C-10				
25_1	9	3	6	66.6	10	3	4	57.1
27_1	8	12	- 4	-50.0	6	4	2	33.3
12_1	16	5	11	68.7	16	5	11	68.7
30_2	11	12	- 1	- 9.0	8	8	0	0
41_2	11	10	1	9.0	11	10	1	9.0
31_2	21	6	15	71.4	31	6	25	80.6
ΣX	76	48	45	156.7	79	36	43	248.7
$\bar{X}$	12.67	8	7.50	26.12	13.17	6	7.17	41.45

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				10-N-10				
4_1	9	17	- 8	- 88.8	10	3	7	70.0
22_1	7	12	- 5	- 71.4	7	7	0	0
29_1	12	5	7	58.3	11	5	6	54.5
46_2	10	3	7	70.0	11	4	7	63.6
37_2	11	8	3	27.2	16	8	8	50.0
ΣX	49	45	4	- 4.7	55	27	28	238.1
$\bar{X}$	9.8	9	0.80	-0.94	11	5.4	5.60	47.62
				10-H-50				
13_1	12	10	2	16.6	11	8	3	27.2
15_1	7	8	- 1	- 14.2	9	7	2	22.2
26_1	10	22	-12	-120.0	22	33	-11	- 50.0
49_2	11	33	-22	-200.0	12	33	-21	-175.0
28_2	13	33	20	-153.8	22	33	-11	- 50.0
ΣX	53	106	-53	-471.4	76	114	-38	-225.6
$\bar{X}$	10.6	21.2	-10.6	-94.28	15.2	22.8	-7.6	-45.12

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				10-C-50				
19_1	7	14	- 7	-100.0	7	17	-10	-142.8
14_1	11	8	3	27.2	10	6	4	40.0
36_2	8	22	-14	-175.0	10	15	- 5	- 50.0
34_2	12	10	2	16.6	16	8	8	50.0
38_2	11	33	-22	-200.0	11	33	-22	-200.0
ΣX	49	87	-38	-431.2	54	79	-25	-302.8
$\bar{X}$	9.8	17.4	-7.60	-86.24	10.8	15.8	-5	-60.56
				10-N-50				
34_1	7	11	- 4	- 57.1	7	11	- 4	- 57.1
43_1	9	10	- 1	- 11.1	6	5	1	16.6
38_1	10	9	1	10.0	12	7	5	41.6
42_2	12	12	0	0	10	15	- 5	- 50.0
47_2	12	9	3	25.0	16	33	-14	- 87.5
ΣX	50	51	- 1	-33.2	51	71	-17	-136.4
$\bar{X}$	10	10.2	-0.20	-6.64	10.2	14.2	-3.40	-27.28

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				50-H-10				
6_1	11	10	1	9.0	10	17	- 7	- 70.0
5_1	18	6	12	66.6	18	8	10	55.5
7_2	9	21	-12	-133.3	9	21	-12	-133.3
13_2	16	9	7	43.7	6	15	- 9	-150.0
19_2	21	18	3	14.2	23	18	5	21.7
17_2	19	9	10	52.6	15	9	6	40.0
9_2	11	28	-17	-154.5	9	33	-24	-266.6
ΣX	105	101	4	-101.7	90	121	-31	-502.7
$\bar{X}$	15	14.43	0.57	-14.53	12.86	17.28	-5.17	-71.81
				50-C-10				
35_1	12	7	5	41.6	10	4	6	60.0
37_1	29	5	24	82.7	12	5	7	58.3
23_1	13	13	0	0.0	12	9	3	25.0
22_2	17	8	9	52.9	17	8	9	52.9
4_2	13	16	- 3	-23.0	13	16	-3	-23.0
1_2	23	11	12	52.1	23	11	12	52.1
ΣX	107	47	47	206.3	87	53	34	225.3
$\bar{X}$	17.83	7.83	7.83	34.38	14.5	8.83	5.67	37.55

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				50-N-10				
11_1	14	17	-3	-21.4	13	17	- 4	- 30.7
18_1	12	5	7	58.3	12	5	7	58.3
23_2	16	7	9	56.2	9	6	3	33.3
12_2	19	16	3	15.7	19	3	16	84.2
16_2	16	20	-4	-25.0	15	20	- 5	- 33.3
5_2	23	22	1	4.3	9	22	-13	-144.4
ΣX	100	87	13	88.1	77	73	4	- 32.6
$\bar{X}$	16.57	14.5	2.17	14.68	12.83	12.17	0.67	-5.43
				50-H-50				
36_1	12	17	- 5	-41.6	9	17	- 8	- 88.8
16_1	13	7	6	46.1	10	4	6	60.0
9_1	25	4	21	84.0	11	12	- 1	- 9.0
20_2	11	16	- 5	-45.4	7	16	- 9	-128.5
14_2	15	15	0	0.0	14	14	0	0.0
24_2	21	33	-12	-57.1	12	33	-21	-175.0
8_2	25	33	- 8	32.0	24	33	- 9	- 37.5
ΣX	122	125	- 3	-46.0	87	129	-42	-378.8
$\bar{X}$	17.43	17.86	-0.43	-6.57	12.43	18.43	-6.0	-54.11

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				50-C-50				
41_1	11	9	2	18.1	9	3	6	66.6
20_1	15	13	2	13.3	16	13	3	18.7
10_1	18	10	8	44.4	18	10	8	44.4
21_2	11	5	6	54.5	15	3	12	80.0
10_2	15	4	11	73.3	19	4	15	78.9
2_2	23	5	18	78.2	23	5	18	78.2
ΣX	93	46	47	281.8	110	38	10.62	366.8
$\bar{X}$	15.5	7.67	7.83	46.97	18.33	6.33	10.33	61.13
				50-N-50				
31_1	12	3	4	33.3	11	3	8	72.7
7_1	15	3	12	80.0	10	5	5	50.0
40_1	22	3	19	86.5	18	3	15	83.3
18_2	14	3	11	80.0	16	3	13	81.2
3_2	15	3	12	80.0	20	3	17	85.0
6_2	15	3	12	80.0	23	3	20	86.9
ΣX	13.83	18	70	438.1	98	20	78	459.1
$\bar{X}$	13.83	3	11.67	73.02	16.33	3.33	13	76.52

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				H-10				
5_2		8				8		
3_2		12				21		
7_2		15				15		
18_2		17				25		
21_2		10				11		
22_2		33				20		
ΣX		95				100		
$\bar{X}$		15.83				16.67		
				C-10				
2_2		32				33		
4_2		19				33		
6_2		12				14		
8_2		12				12		
16_2		13				12		
20_2		16				12		
24_2		12				12		
ΣX		116				128		
$\bar{X}$		16.57				18.28		

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
				N-10				
39_1		6				6		
21_1		11				11		
45_2		8				8		
43_1		12				11		
32_2		10				10		
25_1		9				7		
27_1		8				6		
12_2		16				16		
30_2		11				8		
41_2		11				11		
31_2		21				31		
4_1		9				10		
22_1		7				7		
29_2		12				11		
46_1		10				11		
37_2		11				16		
13_1		12				11		
15_1		7				9		

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
26_1		10				22		
49_2		11				12		
28_2		13				22		
19_1		7				7		
14_1		11				10		
36_2		8				10		
34_1		12				16		
38_2		11				11		
47_2		12				16		
42_2		12				10		
38_1		10				12		
43_2		9				6		
34_2		7				7		
ΣX		324				361		
$\bar{X}$		10.38				9.93		
				H-50				
9_2		29				33		
10_2		33				33		
17_2		16				23		

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
31_2		33				33		
25_2		21				22		
ΣX		132				144		
$\bar{X}$		26.4				28.8		
				C-50				
11_2		33				14		
14_2		12				12		
15_2		14				14		
27_2		23				23		
28_2		33				33		
29_2		24				12		
ΣX		139				108		
$\bar{X}$		23.16				18		
				N-50				
6_1		11				10		
5_2		18				18		
7_1		9				9		
13_2		16				6		
19_2		21				23		

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings
17_2		19				15		
9_1		11				9		
35_1		12				10		
37_1		29				12		
23_1		13				12		
22_2		17				17		
4_2		13				13		
1_2		23				23		
11_1		14				13		
18_2		12				12		
23_2		16				9		
12_2		19				19		
16_2		16				15		
5_1		23				9		
36_1		12				9		
16_1		13				10		
9_2		25				11		
20_1		11				7		
14_2		15				14		

Animal number	Latency ratios				Response ratios			
	Pre-op. acquisition	Post-op. acquisition	Difference score	% savings	Pre-op. acquisition	Post op. acquisition	Difference score	% savings
24_2		21				12		
8_2		25				24		
41_1		11				9		
20_2		15				16		
10_1		18				18		
21_2		11				15		
10_1		15				19		
2_2		23				23		
31_1		12				11		
7_1		15				10		
40_2		22				18		
18_1		14				16		
3_2		15				20		
6_2		15				23		
ΣX		610				549		
$\bar{X}$		16.05				14.45		

Note: Due to the large number of animals used in this experiment, it was necessary to run them in two replications. The animal number subscripts indicate to which replication the animal belonged.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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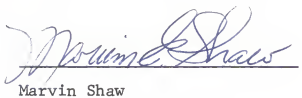

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